REMARKS/ARGUMENTS

Claims 1 to 11 are pending in the instant application. Claim 1 has been amended to particularly point out and distinctly claim that which Applicants consider to be their invention. Claims 2 and 3 have been cancelled and claims 4 and 7 and 9 – 11 have been amended.

Current claim 4 reads on the preferred items of previously presented claim 4. In addition, a typo has been corrected in that diclycolyl now reads diglycolyl.

Claim 7 has been corrected by adding "wherein the asterix * denotes an amine group". Basis for the correction is found in the specification on page 8, line 4 as filed.

Claims 9 – 11 have been amended by including references to claim 1.

New claims 12 to 15 are added.

The following remarks, in conjunction with the above-mentioned amendments, are believed to be fully responsive to the Office Action dated August 30, 2007.

DOUBLE PATENTING REJECTIONS SHOULD BE WITHDRAWN

Claims 1-7 and 9-11 are rejected on the ground of non-statutory obviousness-type double patenting over claims 1 to 4 of U.S. Patent 6,264,914 since they are considered not patentably distinct from each other.

Claims 1-7 and 9-11 are further rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1 to 10 of U.S. Patent 6,921,525 since they are considered not patentably distinct from each other.

Claims 1-7 and 9-11 are still further rejected on the ground of non-statutory obviousness-type double patenting over claims 1 to 5 of U.S. Patent 7,182,934 since they are considered not patentably distinct from each other.

Applicants hold that since the amendments introduced with the claims presently on file these non-statutory obviousness-type double patenting rejections are no longer valid and should be withdrawn.

Claims 1-7 and 9-11 are provisionally rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1 to 10 of copending Application No. 10/541,949. Although the present application teaches the same chelators, imaging moieties and vectors, the linkers (L) are clearly different. With the amendments in the claims applicants find that the double patenting rejections are no longer valid. The provisionally double patenting rejection should therefore be withdrawn.

CLAIM REJECTION UNDER 35 U.S.C. §112

SHOULD BE WITHDRAWN

Claims 1 and 3 - 7 and 9 - 11 are rejected under 35 U.S.C. §112.

Claim 1 is amended and restricted by incorporating previous claims 2 and 3 and part of previous claim 4 into claim 1. Claim 1 is further specified by that a leucine group is linked directly to the group V. Amended claim 1 now specifies that V is an organic group having binding affinity for an angiotensin II receptor site and is Losartan, Valsartan, Candesartan or Eprosartan and that L is a linear or branched amino acid-comprising biomodifier or linker moiety comprising 1-40 amino-acid residues and optionally comprising one or more dicarboxylic acid units, ethyleneglycol units or PEG-like components or combinations thereof, provided that a leucine group is linked directly to the group V. Basis for the provisio that a leucine group is linked directly to the group V is found in examples 1, 4, 7 – 15 and 19 to 46 of the Specification as filed.

Claim 1 is further amended to specify that R is a reporter moiety detectable in *in vivo* imaging of a human or animal body, and where the reporter moiety comprises a metal entity M then R is Y_1M where Y_1 is a chelating agent. Basis for this amendment is found at page 6, lines 15 to 29 of the specification.

Claims 2 – 3 and claim 4 in part are deleted.

Claims 6 and 7 are rejected for having insufficient antecedent basis for the limitation "chelating agent". As explained under the amendments performed in claim 1 above, claims 6 and 7 now have sufficient antecedent basis in claim 1.

Claim 4 is rejected since the phrase "PEG-like components" is considered unclear. This expression is now part of claim 1 and is restricted to read "PEG components". Basis for this restriction is found on page 12, lines 46 to 47 where it is stated that these components can be PEG or PEG like units.

Claims 9 – 11 are amended to be dependent on claim 1.

New claims 12 to 15 are added. Basis for claims 12 to 14 is found at page 12, lines 43 and 44 of the specification. Basis for claim 15 is found at page 12, lines 44 to 47 of the specification.

Applicants therefore hold that the main point of the claims are now clearly set forth, and that the scope of the claims is finite and have support in the specification.

REJECTION UNDER 35 U.S.C. §102 SHOULD BE WITHDRAWN

Claims 1- 3, 9, and 10 stand rejected under 35 U.S.C 102(b) as being anticipated by Klaveness et al. (US 6,264,914).

As noted above, claim 1 has been amended to more particularly claim the present invention. Claim 1 has been restricted by incorporating subject matter of claims 2 and 3 and claim 4 partly. It is correct that Klaveness et al. discloses compositions of the formula V-R-L with the meanings of V, R and L as stated in the Office Action. It is also correct that

Losartan is specifically mentioned as a meaning of the vector V and that the linker L may contain a spacer element of amino acids and that the reporter group R includes chelated metal radionuclides.

However, although Klaveness et al. mentions a wide variety of linkers in column 9, line 65 to column 22, line 34, this publication does not mention compounds where a leucin entity of the linker unit L is linked to the vector (V) moiety.

Thus, Applicants respectfully submit that the present invention as set forth in the enclosed amended claims is novel over the Klaveness et al. disclosure. Reconsideration and withdrawal of this rejection is respectfully requested.

REJECTION UNDER 35 U.S.C. §103 SHOULD BE WITHDRAWN

Claims 1- 3, 6, 7 and 9 to 11 stand rejected under 35 U.S.C 103(a) as being unpatentable over Klaveness et al. (US 6,264,914) in view of Archer et al. (WO 03/006070). This rejection is respectfully traversed.

Klaveness et al. discloses compositions of the formula V-L-R, but does not disclose compounds with a linker L having a leucine group linked directly to the group V. It should be noted that Example 2 of Klaveness does not have a leucine moiety in this position. Archer et al. does not teach a biological targeting moieties having binding affinity to the angiotensin II receptor such as Losartan, Valsartan, Candesartan and Eprosartan. Archer does also not

teach compounds with linker moieties being branched amino acid-comprising biomodifier or linker moiety comprising 1-40 amino-acid residues and optionally comprising one or more dicarboxylic acid units, ethyleneglycol units or PEG-like components or combinations thereof, provided that a leucine group is linked directly to the group V. The linkers proposed by Archer et al. e.g. in claim 1 does not contain amino acids, let alone that a leucine moiety that is linked directly to the group V. It would not be obvious to the skilled man in the art to construct such linkers such as those of the current amended claim 1 since there are no teaching that such linkers contribute to superior properties of the compounds of formula (I). Therefore, the subject matter as a whole would not have been obvious at the time the invention was made to a person having ordinary skill in the art.

Claims 1- 5, 6, 9 and 11 stand rejected under 35 U.S.C 103(a) as being unpatentable over Klaveness et al. (US 6,264,914) in view of Pastan et al. (US 20040018203) and Arbogast et al. (US 7,211,240). This rejection is respectfully traversed.

Applicants are aware that Klaveness et al. proposes that the linker among many other alternatives may be a peptide moiety. Pastan (US 2004/0018203) discloses immunoconjugate where the linker (called connector) between a targeting molecule and an effector molecule may comprise one or more PEG molecules. Such constructs are said to have increased circulation time. Arbogast (US 7,211,240) further discloses multivalent constructs where the chelators are linked to targeting moieties. Neither Klaveness, Pastan or Arbogast describes a linker entity as the one in amended claim 1 (L is a linear or branched amino acid-comprising biomodifier or linker moiety comprising 1-40 amino-acid residues

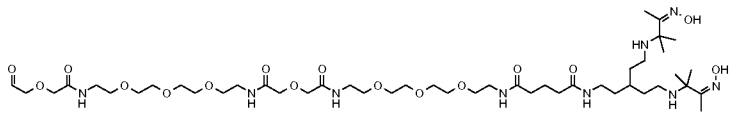
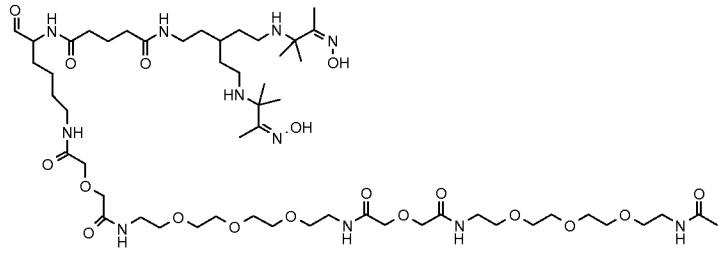
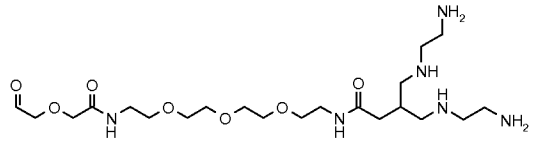
and optionally comprising one or more dicarboxylic acid units, ethyleneglycol units or PEG components or combinations thereof, provided that a leucine group is linked directly to the group V, or even hints to that such linkers may be made and may have improved properties with regards to binding specificity.

It would not be obvious to one skilled in the art to construct such linkers as those of current amended claim 1 since there are no teachings that such linkers contribute to superior properties of the compounds of formula (I). Therefore, the subject matter as a whole would not have been obvious at the time the invention was made to a person having ordinary skill in the art.

Applicants have also found that the L moiety of the present invention strongly affects the binding affinity of the V moiety for the angiotensin II receptor site i.e. the binding affinity is increased compared with angiotensin or Losartan themselves.

The binding affinities for the AT1 receptor were compared by determination of the Ki values in competitive binding assays. Methods for carrying out such competition assays are well known in the art.

The Ki for Losartan and angiotensin II were 10.53 nM and 4.68 respectively. In the table below the Ki value for the compounds of Examples 34, 35 and 43 of the specification are given, and they show a pronounced increase in binding affinity.

Compounds 34, 35 and 43 of table 2	Abbr	AT1 Ki mM
	Losartan-Leu-[Diglycoloyl-PEG(4)]2-Glutaryl-cPn216	0.55
	Losartan-Leu-Lys([Diglycoloyl-PEG(4)]2-Ac)-Glutaryl-cPn216	2.1
	Losartan-Leu-Diglycoloyl-PEG(4)-Tetraamine	0.06

The inventive contribution to the art of the present invention is the finding of compounds suitable for in vivo imaging of AT1 receptor sites. In *in vivo* imaging the binding affinity of the contrast agent to the target receptor is a crucial feature for a suitable contrast agent. The applicant is of the opinion that the fact that the compounds of the present invention exhibit a high affinity for the AT1 receptor proves that the present invention is unobvious in view of the cited prior art.

Based on the above Applicants hold that claims 1-15 are patentable over the cited prior art.

Claims 1- 3 and 9 -11 stand rejected under U.S.C 103(a) as being unpatentable over Klaveness et al. (US 6,264,914) in view of Yang et al. (US 6,692,724). This rejection is respectfully traversed.

Applicants are aware that kits for preparations of radiopharmaceuticals are generally known from the state of art and will point out that only claim 11 as originally filed claims kits. However, Examiner concludes that it would be obvious to one of ordinary skill in the art at the time of the invention to provide compositions of Klaveness in the form of a kit comprising specified chemicals. Applicants cannot see that it is necessary to comment on this matter since amended claim 11 now discloses a kit for the preparation of a radiopharmaceutical composition of formula I of claim 1 comprising a ligand-chelate conjugate and a reducing agent. Hence, the patentability of pending claim 11 depends on the patentability of the compounds of formula I of claim 1 and Applicants believe that claim 11 is patentable together with claim 1.

CLAIM OBJECTION

Applicants have corrected "diclycolyl" in claim 1 to read "diglycolyl".

Applicants note that the Examiner confirms the patentability of claim 8 if rewritten as

an independent claim.

CONCLUSION

Applicants respectfully hold that the amended claims submitted herewith fulfill the requirements of a patentable invention and that all rejections and objections be withdrawn.

The Examiner is invited to telephone the undersigned in order to resolve any issues that might arise and to promote the efficient examination of the current application.

Respectfully submitted,

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